EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L2	16882	coumadin or coumarin	US-PGPUB; USPAT	OR	OFF	2006/07/28 13:00
L3	408	l2 and (low adj dose)	US-PGPUB; USPAT	OR	OFF	2006/07/28 13:00
L4	2963	thromboembolism or (venous adj thromboembolism)or vte	US-PGPUB; USPAT	OR	OFF	2006/07/28 13:01
L5	32	l3 and l4	US-PGPUB; USPAT	OR	OFF	2006/07/28 13:01
S16	1	"6737441".pn.	US-PGPUB; USPAT	OR	OFF	2006/07/27 18:41
S17	0	"10841709".pn.	US-PGPUB; USPAT	OR	OFF	2006/07/27 18:42
S18	1	"6780889".pn.	US-PGPUB; USPAT	OR	OFF	2006/07/27 19:39
S19	17	low adj2 warfarin	US-PGPUB; USPAT	OR	OFF	2006/07/27 19:43
S20	28	ridker and warfarin	US-PGPUB; USPAT	OR	OFF	2006/07/27 19:41
S21	502	bristol and warfarin	US-PGPUB; USPAT	OR	OFF	2006/07/27 19:42
S22	2	S21 and myer	US-PGPUB; USPAT	OR	OFF	2006/07/27 19:41
S23	482	bristol-myers and warfarin	US-PGPUB; USPAT	OR	OFF	2006/07/27 19:42
S24	6515	bristol-myers	US-PGPUB; USPAT	OR	OFF	2006/07/27 19:42
S25	482	S24 and warfarin	US-PGPUB; USPAT	OR	OFF	2006/07/27 19:42
S26	47	S25 and (low adj3 dose)	US-PGPUB; USPAT	OR	OFF	2006/07/27 19:42
S27	17	low adj2 warfarin	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/07/27 21:58

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS	4	APR 04	STN AnaVist $500 visualization usage credit offered
NEWS	5	MAY 10	CA/CAplus enhanced with 1900-1906 U.S. patent records
NEWS	6	MAY 11	KOREAPAT updates resume
NEWS	7	MAY 19	Derwent World Patents Index to be reloaded and enhanced
NEWS	8	MAY 30	IPC 8 Rolled-up Core codes added to CA/CAplus and USPATFULL/USPAT2
NEWS	9	MAY 30	The F-Term thesaurus is now available in CA/CAplus
NEWS	10	JUN 02	The first reclassification of IPC codes now complete in INPADOC
NEWS	11	JUN 26	TULSA/TULSA2 reloaded and enhanced with new search and and display fields
NEWS	12	JUN 28	Price changes in full-text patent databases EPFULL and PCTFULL
NEWS	13	JUl 11	CHEMSAFE reloaded and enhanced
NEWS	14	JUl 14	FSTA enhanced with Japanese patents
NEWS	15	JUl 19	Coverage of Research Disclosure reinstated in DWPI

NEWS EXPRESS JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

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FILE 'HOME' ENTERED AT 12:52:44 ON 28 JUL 2006

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 12:52:57 ON 28 JUL 2006

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 27 JUL 2006 HIGHEST RN 896463-29-9
DICTIONARY FILE UPDATES: 27 JUL 2006 HIGHEST RN 896463-29-9

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TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

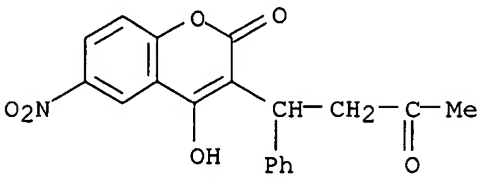
REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> s warfarin
L1 74 WARFARIN

=> d 70-74

L1 ANSWER 70 OF 74 REGISTRY COPYRIGHT 2006 ACS on STN
RN 1641-04-9 REGISTRY
ED Entered STN: 16 Nov 1984
CN 2H-1-Benzopyran-2-one, 4-hydroxy-6-nitro-3-(3-oxo-1-phenylbutyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Coumarin, 3-(α-acetonylbenzyl)-4-hydroxy-6-nitro- (7CI, 8CI)
OTHER NAMES:
CN 3-(1α-Phenyl-β-acetylethyl)-4-hydroxy-6-nitrocoumarin
CN 6-Nitrowarfarin
FS 3D CONCORD
MF C19 H15 N O6
LC STN Files: CA, CAOLD, CAPLUS

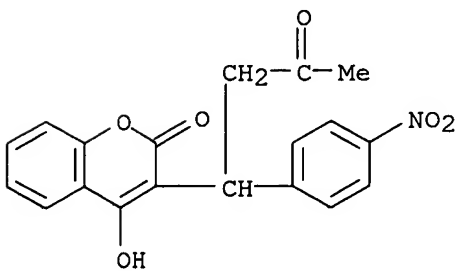


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L1 ANSWER 71 OF 74 REGISTRY COPYRIGHT 2006 ACS on STN
RN 152-72-7 REGISTRY
ED Entered STN: 16 Nov 1984
CN 2H-1-Benzopyran-2-one, 4-hydroxy-3-[1-(4-nitrophenyl)-3-oxobutyl]- (9CI)

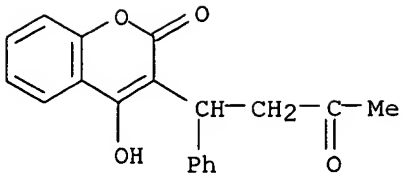
(CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Acenocoumarol (6CI)
CN Coumarin, 3-(α-acetonyl-p-nitrobenzyl)-4-hydroxy- (8CI)
OTHER NAMES:
CN (±)-Acenocoumarin
CN (±)-Acenocoumarol
CN (±)-Nicoumalone
CN (±)-p-Nitrowarfarin
CN 3-(α-Acetonyl-4-nitrobenzyl)-4-hydroxycoumarin
CN 3-(α-Acetonyl-p-nitrobenzyl)-4-hydroxycoumarin
CN 3-(α-p-Nitrophenyl-β-acetylethyl)-4-hydroxycoumarin
CN 3-(Alpha-acetonyl-4-nitrobenzyl)-4-hydroxycoumarin
CN 3-[α-(4'-Nitrophenyl)-β-acetylethyl]-4-hydroxycoumarin
CN 3-[α-(p-Nitrophenol)-β-acetylethyl]-4-hydroxycoumarin
CN 3-[2-Acetyl-1-(p-nitrophenyl)ethyl]-4-hydroxycoumarin
CN 4-Hydroxy-2-oxo-3-[3-oxo-1-(4-nitrophenyl)butyl]-2H-chromene
CN Acenocoumarin
CN Ascumar
CN DL-3-(α-Acetonyl-4-nitrobenzyl)-4-hydroxycoumarin
CN G 23,350
CN G 23350
CN Minisintrom
CN Nicoumalone
CN Nitrowarfarin
CN Sincoumar
CN Sinkumar
CN Sinthrom
CN Sinthrome
CN Sintrom
CN Sintrom Mitis
CN Sintroma
CN Syncoumar
CN Syncumar
CN Syntrom
CN Trombostop
CN Zotil
FS 3D CONCORD
DR 70897-81-3
MF C19 H15 N O6
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, DDFU, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, PIRA, PROMT, PS, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

481 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
481 REFERENCES IN FILE CAPLUS (1907 TO DATE)
44 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L1 ANSWER 72 OF 74 REGISTRY COPYRIGHT 2006 ACS on STN
RN 129-06-6 REGISTRY
ED Entered STN: 16 Nov 1984
CN 2H-1-Benzopyran-2-one, 4-hydroxy-3-(3-oxo-1-phenylbutyl)-, sodium salt (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Coumarin, 3-(α-acetonylbenzyl)-4-hydroxy-, sodium salt (8CI)
CN Warfarin, sodium deriv. (6CI)
OTHER NAMES:
CN (±)-Warfarin sodium
CN 3-(α-Acetonylbenzyl)-4-hydroxycoumarin sodium
CN Aldocumar
CN Athrombin
CN Coumadan Sodico
CN Coumadin
CN Coumadin sodium
CN Coumadine
CN Coumafene sodium
CN Dimantil
CN Farin
CN Marevam
CN Marevan
CN Orfarin
CN Panwarfin
CN Prothromadin
CN Ratsul Soluble
CN Simarc 2
CN Sodium coumadin
CN Sodium warfarin
CN Sodium, [[2-oxo-3-(3-oxo-1-phenylbutyl)-2H-1-benzopyran-4-yl]oxy]-
CN Sofarin
CN Taro-warfarin
CN Tintorane
CN UniWarfin
CN Varfine
CN Waran
CN Warfarin sodium
CN Warfarin sodium salt
CN Warfarina
CN Warfil 5
CN Warfilone
CN Zoocoumarin sodium salt
DR 859043-62-2, 12795-55-0, 51821-81-9
MF C19 H16 O4 . Na
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, EMBASE, HSDB*, IMSCOSEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, PIRA, PROMT, PS, RTECS*, SCISEARCH, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
CRN (81-81-2)

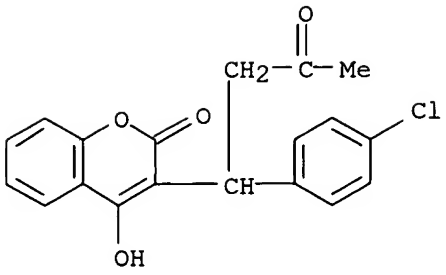


● Na

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

494 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
495 REFERENCES IN FILE CAPLUS (1907 TO DATE)
33 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L1 ANSWER 73 OF 74 REGISTRY COPYRIGHT 2006 ACS on STN
RN 81-82-3 REGISTRY
ED Entered STN: 16 Nov 1984
CN 2H-1-Benzopyran-2-one, 3-[1-(4-chlorophenyl)-3-oxobutyl]-4-hydroxy- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Coumachlor (6CI)
CN Coumarin, 3-(α-acetonyl-p-chlorobenzyl)-4-hydroxy- (7CI, 8CI)
OTHER NAMES:
CN (±)-3-(α-Acetonyl-4-chlorobenzyl)-4-hydroxy coumarin
CN (±)-Coumachlor
CN (±)-p-Chlorowarfarin
CN 3-(α-Acetonyl-4-chlorobenzyl)-4-hydroxycoumarin
CN 3-(α-p-Chlorophenyl-β-acetylethyl)-4-hydroxycoumarin
CN 3-[1-(p-Chlorophenyl)-2-acetylethyl]-4-hydroxycoumarin
CN Cumachlor
CN DL-3-(α-Acetonyl-4-chlorobenzyl)-4-hydroxycoumarin
CN Experimental Rodenticide 332
CN Geigy Rodenticide Exp. 332
CN p-Chlorowarfarin
CN Racemic coumachlor
CN Tomorin
FS 3D CONCORD
DR 128660-48-0, 95041-39-7
MF C19 H15 Cl O4
CI COM
LC STN Files: AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CSCHEM, DDFU, DRUGU, EMBASE, HSDB*, IPA, MEDLINE, MRCK*, MSDS-OHS, RTECS*, SPECINFO, TOXCENTER, ULIDAT, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

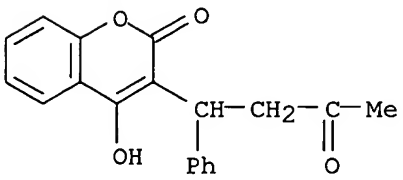


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

189 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
190 REFERENCES IN FILE CAPLUS (1907 TO DATE)
25 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L1 ANSWER 74 OF 74 REGISTRY COPYRIGHT 2006 ACS on STN
RN 81-81-2 REGISTRY
ED Entered STN: 16 Nov 1984
CN 2H-1-Benzopyran-2-one, 4-hydroxy-3-(3-oxo-1-phenylbutyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Coumarin, 3-(α-acetonylbenzyl)-4-hydroxy- (7CI, 8CI)
OTHER NAMES:
CN (±)-Warfarin
CN (±)-Warfarin-alcohol
CN (RS)-Warfarin
CN 1-(4'-Hydroxy-3'-coumarinyl)-1-phenyl-3-butanone
CN 3-(α-Acetonylbenzyl)-4-hydroxycoumarin
CN 3-(α-Phenyl-β-acetylethyl)-4-hydroxycoumarin
CN 3-(1'-Phenyl-2'-acetylethyl)-4-hydroxycoumarin
CN 4-Hydroxy-3-(3-oxo-1-phenylbutyl)-2H-chromen-2-one
CN Athrombine-K
CN Brumolin
CN Co-Rax
CN Compound 42
CN Coumafen
CN Coumafene
CN Coumaphen
CN Coumefene
CN Dethmor
CN DL-3-(α-Acetonylbenzyl)-4-hydroxycoumarin
CN Kumader
CN Kumadu
CN Kumatox
CN NSC 59813
CN rac-Warfarin
CN Ratron
CN Ratron G
CN Rodafarin
CN Rodafarin C
CN Rodex
CN Temus W
CN Vampirinip II
CN Vampirinip III
CN W.A.R.F. 42
CN Warf 5
CN WARF compound 42
CN Warfarin

CN Zoocoumarin
FS 3D CONCORD
DR 56573-89-8, 5543-56-6
MF C19 H16 O4
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, PIRA, PROMT, PS, RTECS*, SCISEARCH, SPECINFO, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4057 REFERENCES IN FILE CA (1907 TO DATE)
57 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
4064 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> file caplus medline bios embase
'BIOS' IS NOT A VALID FILE NAME
Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files that are available. If you have requested multiple files, you can specify a corrected file name or you can enter "IGNORE" to continue accessing the remaining file names entered.
ENTER A FILE NAME OR (IGNORE):file caplus medline bios embase
'FILE' IS NOT A VALID FILE NAME
Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files that are available. If you have requested multiple files, you can specify a corrected file name or you can enter "IGNORE" to continue accessing the remaining file names entered.
ENTER A FILE NAME OR (IGNORE):end

=> file caplus medline biosis embase

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	15.14	15.35

FILE 'CAPLUS' ENTERED AT 12:54:00 ON 28 JUL 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE 'MEDLINE' ENTERED AT 12:54:00 ON 28 JUL 2006

FILE 'BIOSIS' ENTERED AT 12:54:00 ON 28 JUL 2006

FILE 'EMBASE' ENTERED AT 12:54:00 ON 28 JUL 2006

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=> s 129-06-6/rn or 152-72-7/rn or coumadin or coumarin or warfarin or
acenocoumarin or acenocoumarol
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
L2      110581 129-06-6/RN OR 152-72-7/RN OR COUMADIN OR COUMARIN OR WARFARIN
               OR ACENOCOUMARIN OR ACENOCOUMAROL

=> s l2 and (low or low dose or small dose or subtherapeutic)
L3       13832 L2 AND (LOW OR LOW DOSE OR SMALL DOSE OR SUBTHERAPEUTIC)

=> s thromboembolism or idiopathic thromboembolism or spontaneous thromboembolism
or venous thromboembolism)
UNMATCHED RIGHT PARENTHESIS 'BOEMBOLISM)'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s thromboembolism or idiopathic thromboembolism or spontaneous thromboembolism
or venous thromboembolism
L4       65360 THROMBOEMBOLISM OR IDIOPATHIC THROMBOEMBOLISM OR SPONTANEOUS
               THROMBOEMBOLISM OR VENOUS THROMBOEMBOLISM

=> s l4 and recurrent
L5        4443 L4 AND RECURRENT

=> s l5 and l3
L6         691 L5 AND L3

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7          451 DUP REM L6 (240 DUPLICATES REMOVED)

=> s l7 and (ins or international normalized ratio)
L8          68 L7 AND (INS OR INTERNATIONAL NORMALIZED RATIO)

=> focus
PROCESSING COMPLETED FOR L8
L9           68 FOCUS L8 1-

=> d ibib abs 1-68

L9   ANSWER 1 OF 68  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:        2006:645209  CAPLUS
TITLE:                   D-dimer, factor VIII coagulant activity, low
                         -intensity warfarin and the risk of
                         recurrent venous
                         thromboembolism
AUTHOR(S):               Shrivastava, S.; Ridker, P. M.; Glynn, R. J.;
                         Goldhaber, S. Z.; Moll, S.; Bounameaux, H.; Bauer, K.
                         A.; Kessler, C. M.; Cushman, M.
CORPORATE SOURCE:        Center for Cardiovascular Disease Prevention, Brigham
                         and Women's Hospital, Boston, MA, USA
SOURCE:                  Journal of Thrombosis and Haemostasis (2006), 4(6),
                         1208-1214
                         CODEN: JTHOA5; ISSN: 1538-7933
PUBLISHER:               Blackwell Publishing, Inc.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   Background: Elevated plasma D-dimer and factor VIII coagulant activity
     (FVIIIc) may be associated with the risk of recurrent
     venous thromboembolism (VTE).  Objectives: To evaluate
     D-dimer and FVIIIc as risk factors for recurrent VTE and assess
```

the efficacy of extended low-intensity warfarin (target International Normalized Ratio 1.5-2.0) in preventing recurrence by biomarker level. Patients and methods: In the Prevention of Recurrent Venous Thromboembolism trial, 508 idiopathic VTE patients treated for ≥ 3 mo with full-intensity warfarin, and who had stopped warfarin for 7 wk on average, were randomized to low -intensity warfarin or placebo and followed for 2.1 years for recurrent VTE. Prerandomization blood samples were analyzed for D-dimer and FVIIIc. Results: One-third of participants had elevated baseline D-dimer (≥ 500 ng mL-1) and one-fourth, elevated FVIIIc (≥ 150 IU dL-1). Adjusting for other risk factors, the hazard ratios (HRs) for recurrent VTE with elevated D-dimer or FVIIIc were 2.0 [95% confidence interval (CI) 1.2-3.4] and 1.5 (95% CI 0.8-2.8), resp. The association of elevated D-dimer with recurrence was larger among patients with one prior VTE (HR 3.2,95% CI 1.3-8.0) than in patients with more than one event (HR 1.4, 95% CI 0.7-2.2). For patients with one prior VTE on placebo, the annual recurrence incidence was 10.9% with elevated D-dimer and 2.9% with normal values. Low-intensity warfarin was equally effective in recurrence risk reduction in those with normal or elevated biomarkers. Conclusions: Among patients with idiopathic VTE, measurement of D-dimer, but not FVIIIc, might be useful for risk stratification. The efficacy of extended low-intensity warfarin therapy did not vary by biomarker level.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 68 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:284293 CAPLUS

DOCUMENT NUMBER: 139:63008

TITLE: Long-term, low-intensity warfarin therapy for the prevention of recurrent venous thromboembolism

AUTHOR(S): Ridker, Paul M.; Goldhaber, Samuel Z.; Danielson, Ellie; Rosenberg, Yves; Eby, Charles S.; Deitcher, Steven R.; Cushman, Mary; Moll, Stephan; Kessler, Craig M.; Elliott, C. Gregory; Paulson, Rolf; Wong, Turnly; Bauer, Kenneth A.; Schwartz, Bruce A.; Miletich, Joseph P.; Bounameaux, Henri; Glynn, Robert J.; Danielson, E. M.; Bates, D.; Christen, W.; DeFonce, P.; Griffin, W.; Jackson, F.; Murray, A.; Taylor, K.; Johnson, K.; McKenna, K.; Pierre, J.; Holman, B.; Dessources, F.; Quinn, P.; Laurinaitis, T.; MacFadyen, J.; Eby, C.; Miletich, J. P.; Porche-Sorbet, R.; Goldhaber, S. Z.; Morrison, R. B.; MacDougall, R. C.; Morrison, R. M.; Lamas, G.; Bailey, K.; Gersh, B.; Pellegrino, E.; Rick, M.; Vaughan, D.; Rosenberg, Y.; Deitcher, S. R.; Olin, J.; Sulzer, S.; Clark, T.; Cushman, M.; Cohen, R.; Moll, S.; Jones, S.; Kessler, C. M.; Lee, A.; Elliott, C. G.; Kitterman, N.; Jafri, S.; Wulbrecht, N.; Bauer, K.; Mahony, M.; Paulson, R.; Vold, D.; Wong, T.; Erickson-Nesmith, S.; Bounameaux, H.; de Lucia, S.; Chagnon, I.; Schwartz, B.; Thackery, R.; Gates, N.; Nguyen, P.; Paris, S.; LeCours, B.; Oliver, M.; Hodapp, K.; Grad, G.; Bank, B.; Rindels, J.; Leano, C.; Haire, W.; O'Grady, D.; Schneider, J.; Key, N.; Christie, B.; Blostein, M.; Strulovitch, C.; Usedom, J.; Oskins, D.; Eby, C.; Lee, V.; Heuerman, S.; Kerins, D.; Roberts, B.; White, R.; Castro, E.; Riddle, E.; Ingram, M.; Becker, R. C.; Emery, C.; Wong, L.; Dent, S.; Comp, P.; Havarda, D.; Galichia, J. P.; Terry, L.; Waldren, S.; Hambleton, J.; Roth,

J.; Pineo, G.; Hull, R.; Sheldon, J.; Tsapatsaris, N.; Woodhead, G.; Mann, M.; Welsh, C.; Schoch, T.; Goldsmith, J.; Anthony, T.; Walters, J.; Caprini, J.; Maher, M. L.; Medica, K.; Rabbitt, S.; Finocchio, J.; Keaton, K.; Lee, H.; McLean, S.; Barban, K.; Mohler, E.; Medenilla, E.; Wolfe, M.; de Lemos, A.; Rubenfite, M.; McDevitt, S.; Housholder, S.; Siegel, J. E.; Bradley, B.; Brophy, M.; Reilly, C.; Brown, E.; Valeria, A.; Rodriguez, L.; Kumar, A.; Pekron, J.; Wagner, J.; Richart, J.; Jones, J.; Weber, V.; Fellin, C.; Sim, J.; Graham, M.; Sutton, D.; Kestin, A.; Tezcan, H.; Herbst, S.; Waldrum, M.; Meadows, T.; Carlson, W.; Welch-Costantino, M.; Gosset, J.; Nonnweiler, J.; Kumar, A.; Green, K.; Tapson, V.; Krichman, A.; Yeo, E.; Boross-Harmer, S.

CORPORATE SOURCE: Center for Cardiovascular Disease prevention and the Divisions of Preventive Medicine and Cardiology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

SOURCE: New England Journal of Medicine (2003), 348(15), 1425-1434
CODEN: NEJMAG; ISSN: 0028-4793
PUBLISHER: Massachusetts Medical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Standard therapy to prevent recurrent venous thromboembolism includes 3 to 12 mo of treatment with full-dose warfarin with a target international normalized ratio (INR) between 2.0 and 3.0. However, for long-term management, no therapeutic agent has shown an acceptable benefit-to-risk ratio. Patients with idiopathic venous thromboembolism who had received full-dose anti- coagulation therapy for a median of 6.5 mo were randomly assigned to placebo or low-intensity warfarin (target INR, 1.5 to 2.0). Participants were followed for recurrent venous thromboembolism, major hemorrhage, and death. The trial was terminated early after 508 patients had undergone randomization and had been followed for up to 4.3 yr (mean, 2.1). Of 253 patients assigned to placebo, 37 had recurrent venous thromboembolism (7.2 per 100 person-years), as compared with 14 of 255 patients assigned to low-intensity warfarin (2.6 per 100 person-years), a risk reduction of 64 percent (hazard ratio, 0.36 [95 percent confidence interval, 0.19 to 0.67]; P<0.001). Risk redns. were similar for all subgroups, including those with and those without inherited thrombophilia. Major hemorrhage occurred in two patients assigned to placebo and five assigned to low -intensity warfarin (P=0.25). Eight patients in the placebo group and four in the group assigned to low-intensity warfarin died (P=0.26). Low-intensity warfarin was thus associated with a 48 percent reduction in the composite end point of recurrent venous thromboembolism, major hemorrhage, or death. According to per-protocol and as-treated analyses, the reduction in the risk of recurrent venous thromboembolism was between 76 and 81 percent. Long-term, low-intensity warfarin therapy is a highly effective method of preventing recurrent venous thromboembolism.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 68 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:639305 CAPLUS
DOCUMENT NUMBER: 139:286043

TITLE: Comparison of low-intensity warfarin

therapy with conventional-intensity warfarin therapy for long-term prevention of recurrent venous thromboembolism

AUTHOR(S): Kearon, Clive; Ginsberg, Jeffrey S.; Kovacs, Michael J.; Anderson, David R.; Wells, Philip; Julian, Jim A.; MacKinnon, Betsy; Weitz, Jeffrey I.; Crowther, Mark A.; Solan, Sean; Turpie, Alexander G.; Geerts, William; Solymoss, Susan; van Nguyen, Paul; Demers, Christine; Kahn, Susan R.; Kassis, Jeannine; Rodger, Marc; Hambleton, Julie; Gent, Michael; Morrow, B.; Kovacs, J.; Moore, M.; Lewis, G.; Colley, M.; Biagioni, L.; Burnett, C.; Stevens, P.; MacLeod, D.; Pleasance, S.; Schnurr, T.; Mayes, C.; Strong, D.; Zondag, M.; Code, K.; Bartle, W.; St. Jacques, B.; Schmaltz, H.; Poulin, J.; Vu, L.; Strulovitch, C.; Elizov, M.; Lecours, B.; Cayer, G.; Radey, L.; Beausoleil, F.; Busque, L.; Tatsuno-Roth, J.; Lychak, T.; Goeree, L.; MacKinnon, B.; Julian, J.; Gent, M.; Weitz, J.; Levine, M.; Hirsh, J.; Douketis, J.; Ginsberg, J.; Johnston, M.; McGrath, J.

CORPORATE SOURCE: The Extended Low-Intensity Anticoagulation for Thrombo-Embolism Investigators, McMaster University, Hamilton, ON, Can.

SOURCE: New England Journal of Medicine (2003), 349(7), 631-639
CODEN: NEJMAG; ISSN: 0028-4793
PUBLISHER: Massachusetts Medical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: Warfarin is very effective in preventing recurrent venous thromboembolism but is also associated with a substantial risk of bleeding. After three months of conventional warfarin therapy, a lower dose of anticoagulant medication may result in less bleeding and still prevent recurrent venous thromboembolism. Methods: We conducted a randomized, double-blind study, in which 738 patients who had completed three or more months of warfarin therapy for unprovoked venous thromboembolism were randomly assigned to continue warfarin therapy with a target international normalized ratio (INR) of 2.0 to 3.0 (conventional intensity) or a target INR of 1.5 to 1.9 (low intensity). Patients were followed for an average of 2.4 yr. Results: Of 369 patients assigned to low-intensity therapy, 16 had recurrent venous thromboembolism (1.9 per 100 person-years), as compared with 6 of 369 assigned to conventional-intensity therapy (0.7 per 100 person-years; hazard ratio, 2.8; 95 % confidence interval, 1.1 to 7.0). A major bleeding episode occurred in nine patients assigned to low-intensity therapy (1.1 events per 100 person-years) and eight patients assigned to conventional-intensity therapy (0.9 event per 100 person-years; hazard ratio, 1.2; 95 % confidence interval, 0.4 to 3.0). There was no significant difference in the frequency of overall bleeding between the two groups (hazard ratio, 1.3; 95 % confidence interval, 0.8 to 2.1). Conventional-intensity warfarin therapy is more effective than low-intensity warfarin therapy for the long-term prevention of recurrent venous thromboembolism. The low-intensity warfarin regimen does not reduce the risk of clin. important bleeding.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 68 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:537906 CAPLUS
DOCUMENT NUMBER: 139:207440

TITLE: Low-molecular-weight heparin versus a coumarin for the prevention of recurrent venous thromboembolism in patients with cancer

AUTHOR(S): Lee, Agnes Y. Y.; Levine, Mark N.; Baker, Ross; Bowden, Chris; Kakkar, Ajay K.; Prins, Martin; Rickles, Frederick R.; Julian, Jim A.; Haley, Susan; Kovacs, Michael J.; Gent, Michael; Levine, M.; Baker, R.; Bowden, C.; Gent, M.; Kakkar, A.; Lee, A.; Prins, M.; Rickles, F.; Pater, J.; Bueller, H.; Goldhaber, S.; Ginsberg, J.; Hirsh, J.; Kearon, C.; Thomson, G.; Weitz, J.; Julian, J.; Haley, S.; Ling, A.; Rush, B.; Finch, T.; Bonella-Escobedo, L.; Matthews, L.; Windsor, J.; Tavormina, C.; Nelson, H.; Lewis, G.; Sicurella, J.; Lee, A.; Booker, N.; Schmidt, S.; Kovacs, M.; Morrow, B.; McCarron, B.; Pleasance, S.; Brien, W. F.; Boross-Harmer, S.; Douketis, J. D.; Schnurr, T.; Solymoss, S.; St. Jacques, B.; Geerts, W.; Code, K.; Chia, S.; Monkman, S.; Turpie, A. G. G.; Johnson, J.; Sutherland, J.; Shori, S.; Baker, R.; Smith, J.; Coghlan, D. W.; Osmond, J. M.; Dunkley, S.; Chong, B.; Salem, H.; Poulton, L.; Hertzberg, M.; Stavros, P.; Ockelford, P.; Rolfe-Vyson, V.; Brighton, T. A.; Ristuccia, R.; Ward, C. M.; Sheather, K.; Olver, L. N.; Marafioti, T.; Ma, D.; Gan, T. E.; Cummins, A.; Grigg, A.; Cinc, E.; Liebman, H.; Weitz, I.; Anderson, M. D.; Escalante, C. P.; Horace, P.; Green, D.; Calimaran, M.; Moll, A.; Jones, S. K.; Stopeck, A.; Glennie, K.; Ribeiro, M.; Starke, L.; Deitcher, S. R.; Lipsey, L.; Brandy, A.; Krishnan, R.; Cushman, M.; Chassereau, L.; Macik, B. G.; Newton, L.; Tarnower, A.; Weiler, R. J.; Cohen, A. J.; White, E.; Bona, R.; Jennings, K.; Falanga, A.; Labianca, R.; Prandoni, P.; Piccioli, A.; Zanon, E.; Federici, A. B.; Pizzocaro, G.; Smorenburg, S. M.; Klerk, C. P. W.; Berkmortel, F.; Wagener, D. J. T.; Erdkamp, F. L. G.; van der Heul, C.; Post, C.; Biesma, D. H.; Kroon, C.; Kamphuis van der Poel, M.; Davant, E.; Monreal, M.; Quigley, M.; Rustin, G. J. S.; Boxall, J.

CORPORATE SOURCE: CLOT Investogators, Department of Medicine, McMaster University, Hamilton, ON, Can.

SOURCE: New England Journal of Medicine (2003), 349(2), 146-153
CODEN: NEJMAG; ISSN: 0028-4793

PUBLISHER: Massachusetts Medical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background: Patients with cancer have a substantial risk of recurrent thrombosis despite the use of oral anticoagulant therapy. We compared the efficacy of a low-mol.-weight heparin with that of an oral anticoagulant agent in preventing recurrent thrombosis in patients with cancer. Methods: Patients with cancer who had acute, symptomatic proximal deep-vein thrombosis, pulmonary embolism, or both were randomly assigned to receive low-mol.-weight heparin (dalteparin) at a dose of 200 IU per kg of body weight s.c. once daily for five to seven days and a coumarin derivative for six months (target international normalized ratio, 2.5) or dalteparin alone for six months (200 IU per kg once daily for one month, followed by a daily dose of approx. 150 IU per kg for five months). Results: During the six-month study period, 27 of 336 patients in the dalteparin group had recurrent venous thromboembolism, as compared with 53 of 336 patients in the oral-anticoagulant group (hazard ratio, 0.48; P=0.002). The probability of

recurrent thromboembolism at six months was 17 % in the oral-anticoagulant group and 9 % in the dalteparin group. No significant difference between the dalteparin group and the oral-anticoagulant group was detected in the rate of major bleeding (6 % and 4 %, resp.) or any bleeding (14 % and 19 %, resp.). The mortality rate at six months was 39 % in the dalteparin group and 41 % in the oral-anticoagulant group. Conclusions: In patients with cancer and acute venous thromboembolism, dalteparin was more effective than an oral anticoagulant in reducing the risk of recurrent thromboembolism without increasing the risk of bleeding.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 68 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:992154 CAPLUS
DOCUMENT NUMBER: 142:328559
TITLE: Low intensity warfarin: is it clinically useful in venous thromboembolism management?
AUTHOR(S): Bauer, Kenneth A.
CORPORATE SOURCE: VA Boston Healthcare System and Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA
SOURCE: British Journal of Haematology (2004), 127(2), 155-158
CODEN: BJHEAL; ISSN: 0007-1048
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Therapy for a first episode of venous thromboembolism (VTE) typically includes a vitamin K antagonist, such as warfarin, for 3-6 mo at an international normalized ratio (INR) of 2-3. After the cessation of warfarin therapy, unprovoked VTE is associated with a recurrence rate of 5-15% per yr. Prolonging initial therapy does not reduce the recurrence risk once warfarin is discontinued and is not routinely recommended for such patients. The Prevention of Recurrent Venous Thromboembolism (PREVENT) and Extended Low-Intensity Anticoagulation for Thromboembolism (ELATE) trials were undertaken to evaluate the efficacy and safety of low-intensity warfarin (INR 5-2) in this population. While both trials demonstrated that low -intensity warfarin offers substantial protection against recurrent VTE, only the ELATE trial included a standard intensity arm; this arm showed a significantly lower recurrence rate and a major bleed rate that, surprisingly, was similar to the low-intensity arm. There still remains no consensus that long-term warfarin at an INR of 2-3 should be recommended for all patients who sustain a first unprovoked venous thromboembolic event, which largely stems from our current inability to reliably identify those patients most likely to develop recurrences. Given that an individualized approach is required in deciding the duration of anticoagulation, it is the author's belief that low-intensity warfarin, which the PREVENT trial demonstrated could be monitored every other month, is a useful option for some patients with a first episode of VTE.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 68 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:408228 CAPLUS
DOCUMENT NUMBER: 139:111365
TITLE: Comparison of 10-mg and 5-mg warfarin initiation nomograms together with low -molecular-weight heparin for outpatient treatment of

acute venous thromboembolism: a randomized, double-blind, controlled trial

AUTHOR(S): Kovacs, Michael J.; Rodger, Marc; Anderson, David R.; Morrow, Beverly; Kells, Gertrude; Kovacs, Judy; Boyle, Eleanor; Wells, Philip S.

CORPORATE SOURCE: FRCPC, Dep. of Hematol., London Health Sci. Cent., London, ON, N6A 4G5, Can.

SOURCE: Annals of Internal Medicine (2003), 138(9), 714-719
CODEN: AIMEAS; ISSN: 0003-4819

PUBLISHER: American College of Physicians-American Society of Internal Medicine

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background: The optimal means of achieving therapeutic oral anticoagulation in the outpatient setting has not been determined Objective: To compare a 10-mg dosing nomogram with a 5-mg nomogram that has been suggested to be sufficient for warfarin initiation. Design: Randomized, controlled clin. trial. Setting: Outpatient venous thromboembolism services of four tertiary care hospitals. Patients: 201 of 210 consecutive patients with objectively confirmed diagnoses of acute venous thromboembolism. Intervention: All patients were treated with s.c. low-mol.-weight heparin for a min. of 5 days until a therapeutic international normalized ratio (INR) was achieved. Patients were randomly assigned to initially receive a 10-mg or 5-mg dose of warfarin. Measurements: The primary end point was time in days to therapeutic INR. Secondary end points were the proportion of patients who had achieved a therapeutic INR by day 5, the total number of INR assessments, the number of INR measurements greater than 5.0, incidence of recurrent venous thromboembolism and major bleeding, and survival. Results: 210 consecutive patients met the inclusion criteria. Of these, 9 were excluded and 201 were randomly assigned to study groups (104 to the 10-mg group and 97 to the 5-mg group). Demog. characteristics of both groups were similar. Patients in the 10-mg group achieved therapeutic INR 1.4 days earlier than patients in the 5-mg group ($P < 0.001$). Eighty-three percent of patients in the 10-mg group achieved a therapeutic INR by day 5 vs. 46% in the 5-mg group ($P < 0.001$). Fewer INR assessments were performed in the 10-mg group than in the 5-mg group (8.1 vs. 9.1; $P = 0.04$). There were no significant differences between the two groups in recurrent events, major bleeding, survival, and number of INR measurements greater than 5.0. Conclusion: The 10-mg warfarin initiation nomogram is superior to the 5-mg nomogram because it allows more rapid achievement of a therapeutic INR.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 68 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:21089 CAPLUS

DOCUMENT NUMBER: 135:102211

TITLE: Clinical risk factors and timing of recurrent venous thromboembolism during the initial 3 months of anticoagulant therapy

AUTHOR(S): Douketis, James D.; Foster, Gary A.; Crowther, Mark A.; Prins, Martin H.; Ginsberg, Jeffrey S.

CORPORATE SOURCE: Departments of Medicine, McMaster University, Can.

SOURCE: Archives of Internal Medicine (2000), 160(22), 3431-3436
CODEN: AIMDAP; ISSN: 0003-9926

PUBLISHER: American Medical Association

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background: In patients with venous thromboembolism

(VTE), identifying clin. risk factors for recurrence during the initial 3 mo of anticoagulant therapy and knowledge of the time course of recurrence may help clinicians decide about the frequency of clin. surveillance and the appropriateness of outpatient treatment. Methods: Anal. of a randomized controlled trial database involving 1021 patients with VTE (750 with deep vein thrombosis [DVT] and 271 with pulmonary embolism [PE]) who were followed up for 3 mo after the start of anticoagulant therapy. All patients received initial treatment with unfractionated heparin or a low-mol.-weight heparin (reviparin) and a coumarin derivative starting the first or second day of treatment, with a target international normalized ratio of 2.0 to 3.0.
Results: Four independent clin. risk factors for recurrent VTE were identified: (1) cancer (odds ratio [OR], 2.72; 95% confidence interval [CI], 1.39-5.32), (2) chronic cardiovascular disease (OR, 2.27; 95% CI, 1.08-4.97), (3) chronic respiratory disease (OR, 1.91; 95% CI, 0.85-4.26), and (4) other clin. significant medical disease (OR, 1.79; 95% CI, 1.00-3.21). Older age was associated with a decreased risk for recurrent VTE (OR, 0.76; 95% CI, 0.64-0.92). Previous VTE, sex, and idiopathic VTE were not risk factors for recurrence. In patients with DVT or PE, there was no significant difference in the rates of recurrent nonfatal VTE (4.8% vs. 4.1%; P=.62), major bleeding (2.9% vs. 2.2%; P=.53), and non-VTE death (6.4% vs. 7.8%; P=.45), but recurrent fatal PE was more frequent in patients with PE than DVT (2.2% vs. 0%; P<.01). There was a clustering of recurrent VTE episodes during the initial 2 to 3 wk after the start of treatment.
Conclusions: During the initial 3 mo of anticoagulant therapy, recurrent VTE is more likely to occur in patients with cancer, chronic cardiovascular disease, chronic respiratory disease, or other clin. significant medical disease. Patients with PE are as likely to develop recurrent VTE as those with DVT; however, recurrence is more likely to be fatal in patients who initially present with PE.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 68 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:113638 CAPLUS
DOCUMENT NUMBER: 142:456599
TITLE: Ximelagatran vs low-molecular-weight heparin and warfarin for the treatment of deep vein thrombosis. A randomized trial
AUTHOR(S): Fiessinger, Jean-Noel; Huisman, Menno V.; Davidson, Bruce L.; Bounameaux, Henri; Francis, Charles W.; Eriksson, Henry; Lundstroem, Tobjoern; Berkowitz, Scott D.; Nystroem, Per; Thorsen, Mona; Ginsberg, Jeffrey S.
CORPORATE SOURCE: THRIVE Treatment Study Investigators, Department of Vascular medicine, Hopital Europeen Georges Pompidou, Paris, Fr.
SOURCE: JAMA, the Journal of the American Medical Association (2005), 293(6), 681-689
CODEN: JAMAAP; ISSN: 0098-7484
PUBLISHER: American Medical Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Context Ximelagatran, an oral direct thrombin inhibitor with a rapid onset of action and predictable antithrombotic effect, has the potential to be a simple therapeutic alternative to current standard treatment of acute venous thromboembolism. Objective To compare the efficacy and safety of ximelagatran with standard enoxaparin/warfarin treatment for the prevention of recurrent venous thromboembolism. Design, Setting, and Patients Randomized, double-blind, non-inferiority trial (Thrombin Inhibitor in Venous Thromboembolism [THRIVE] Treatment Study) of 2489 patients with

acute deep vein thrombosis, of whom approx. one third had concomitant pulmonary embolism. The study was conducted at 279 centers in 28 countries from Sept. 2000 through Dec. 2002. Interventions Patients were randomized to receive 6 mo of treatment with either oral ximelagatran, 36 mg twice daily, or s.c. enoxaparin, 1 mg/kg twice daily, for 5 to 20 days followed by warfarin adjusted to maintain an international normalized ratio of 2.0 to 3.0. Main Outcome Measures Recurrent venous thromboembolism, bleeding, and mortality. Results Venous thromboembolism recurred in 26 of the 1240 patients assigned to receive ximelagatran (estimated cumulative risk, 2.1%) and in 24 of the 1249 patients assigned to receive enoxaparin/warfarin (2.0%). The absolute difference between ximelagatran and enoxaparin/warfarin was 0.2% (95% confidence interval [CI], -1.0% to 1.3 %). This met the prespecified criterion for non-inferiority. Corresponding values for major bleeding were 1.3% and 2.2% (difference, -1.0%; 95% CI, -2.1 % to 0.1 %), and for mortality were 2.3% and 3.4% (difference, -1.1 %; 95% CI, -2.4% to 0.2%). Alanine aminotransferase levels increased to more than 3 times the upper limit of normal in 119 patients (9.6%) and 25 patients (2.0%) receiving ximelagatran and enoxaparin/warfarin, resp. Increased enzyme levels were mainly asymptomatic. Retrospective anal. of locally reported adverse events showed a higher rate of serious coronary events with ximelagatran (10/1240 patients) compared with enoxaparin/ warfarin (1/1249 patients). Conclusions Oral ximelagatran administered in a fixed dose without coagulation monitoring, was as effective as enoxaparin/warfarin for treatment of deep vein thrombosis with or without pulmonary embolism and showed similar, low rates of bleeding. Increased levels of liver enzymes in 9.6% of ximelagatran-treated patients require regular monitoring; the mechanism requires further evaluation. Prospective assessment of coronary-events in future studies is warranted.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 68 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:447431 CAPLUS
DOCUMENT NUMBER: 125:131373
TITLE: Prevention and treatment of venous thromboembolism
AUTHOR(S): Pineo, Graham F.; Hull, Russell D.
CORPORATE SOURCE: Calgary General and Foothills Hospitals, University Calgary, Calgary, AB, Can.
SOURCE: Drugs (1996), 52(1), 71-92
CODEN: DRUGAY; ISSN: 0012-6667
PUBLISHER: Adis
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 163 refs. All patients at moderate to high risk for the development of venous thromboembolism should receive prophylaxis. The approaches of proven value include low-dose heparin, low mol. weight heparin, oral anticoagulants and intermittent pneumatic compression. The use of one of the cited heparin nomograms will ensure that all patients are rapidly brought within the therapeutic range. Because of the varying sensitivities of thromboplastins, each laboratory should establish a therapeutic range using the activated partial thromboplastin time (APTT) which will correspond to 0.2 to 0.4 U/mL of heparin. Constant vigilance and a high level of suspicion are necessary to establish the clin. diagnosis of heparin-induced thrombocytopenia, and to institute appropriate therapy. Physicians should be aware of the sensitivity of the thromboplastin being used in the performance of the International Normalized Ratio (INR). Care must be taken to ensure that patients are maintained within the target therapeutic range for INR (in most cases 2 to

3) by frequent determination of the INR and appropriate adjustments of warfarin dosage. Low mol. weight heparin is the recommended approach to the initial management of venous thromboembolism where these agents are available. Patients with an acute episode of venous thromboembolism should receive warfarin therapy for at least 3 mo. At the present time it is reasonable to treat the first recurrence with oral anticoagulants for a period of 12 mo and indefinitely for more than 1 recurrence. For selected patients with acute massive pulmonary embolism, thrombolytic therapy with one of the available agents is recommended. However, the role of thrombolytic therapy in patients with proximal venous thrombosis remains unclear. In selected patients with acute venous thromboembolism who have contra-indications to anticoagulant therapy or who have objectively documented recurrent disease while on adequate therapy, the insertion of an inferior vena cava filter is recommended.

L9 ANSWER 10 OF 68 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:796968 CAPLUS
DOCUMENT NUMBER: 123:188152
TITLE: Optimal duration of oral anticoagulant therapy: a randomized trial comparing four weeks with three months of warfarin in patients with proximal deep vein thrombosis
AUTHOR(S): Levine, Mark N.; Hirsh, Jack; Gent, Michael; Turpie, Alexander G.; Weitz, Jeffrey; Ginsberg, Jeffrey; Geerts, William; LeClerc, Jacques; Neemeh, Jean; et al.
CORPORATE SOURCE: Dep. Med. Clinical Epidemiology & Biostatistics, McMaster Univ., Hamilton, ON, Can.
SOURCE: Thrombosis and Haemostasis (1995), 74(2), 606-11
CODEN: THHADQ; ISSN: 0340-6245
PUBLISHER: Schattauer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The optimal duration of oral anticoagulant therapy for patients with acute proximal deep vein thrombosis (DVT) is uncertain. Based on the hypothesis that a normal impedance plethysmogram (IPG) following DVT defines a group of patients at low risk of recurrent venous thromboembolism (VTE), a trial was conducted to evaluate the efficacy of only four weeks of warfarin. Patients with venog. confirmed acute proximal DVT who had received four weeks of warfarin after initial heparin and whose four week IPG was normal were allocated to either continue warfarin (targeted International Normalized Ratio 2.0 to 3.0) for a further eight weeks or receive placebo. Patients with an abnormal four week IPG received warfarin for a further eight weeks. Based on clin. characteristics at the time of the qualifying thrombosis, all patients were classified as having either continuing or transient risk factors for recurrent VTE. During the eight weeks following randomization, nine (8.6%) of the 105 placebo patients developed recurrent VTE compared to one (0.9%) of the 109 warfarin patients, P = 0.009. Over the entire 11 mo of follow-up, 12 placebo patients developed recurrence compared to one (0.9%) of the 109 warfarin patients, P = 0.009. Over the entire 11 mo of follow-up, 12 placebo patients developed recurrence compared to seven warfarin patients, P = 0.3. Nineteen of the 192 patients with an abnormal four week IPG experienced recurrence during the nine months after discontinuing warfarin. In the 301 patients who received three months of warfarin in the randomized trial or in the cohort study, all 26 recurrent events were in the 212 patients with continuing risk factors. In conclusion, an IPG four weeks after proximal DVT is not a useful predictor for recurrent VTE; whereas the

presence of continuing risk factors is a very strong predictor. Four weeks of oral anticoagulants may be all that is required in patients without continuing risk factors. Patients with continuing risk factors may require more than three months of oral anticoagulants.

L9 ANSWER 11 OF 68 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:19753 CAPLUS
DOCUMENT NUMBER: 139:254997
TITLE: Experiences of a low-intensity anticoagulation regimen for extended secondary prevention of venous thromboembolism
AUTHOR(S): Svensson, Per; Soedermark, Anna; Schulman, Sam
CORPORATE SOURCE: Dept of Medicine, Division of Emergency Medicine, Karolinska Hospital, Stockholm, Swed.
SOURCE: Hematology Journal (2002), 3(6), 311-314
CODEN: HJEOBZ; ISSN: 1466-4860
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Extended treatment with vitamin K antagonists for more than 6 mo is often used for secondary prevention of venous thromboembolism (VTE) in patients at high or moderate risk for recurrent events. The intensity of anticoagulant therapy is usually maintained at an International Normalized Ratio (INR) of 2-3. An INR of 1.5-2 might also prevent thromboembolic events with less complications of bleeding, but results from randomized trials are not yet available. In a non-prospective, uncontrolled study 40 patients with a history of VTE and an estimated high risk for recurrent events due to several previous events and/or thrombophilic defects were, after a median of 11.5 mo on regular intensity anticoagulation (INR 2-3), switched to a low intensity regimen (INR 1.5-2). In six of the patients an estimated high risk for complications of bleeding contributed to this decision. After a median follow-up of 36 mo (140 patient-years) recurrent events, complications of bleeding and some basic quality of life measurements regarding the new treatment were registered. No recurrent events, four minor bleedings and no major bleedings were registered. Twenty-six patients preferred an INR of 1.5-2 compared to 2-3. The main reasons for that preference were a lower risk for bleeding (13 patients) and less frequent monitoring of the INR (18 patients). No patient preferred full-dose anticoagulation at INR 2-3. In patients at a high risk for recurrence of VTE an initial period of regular intensity anticoagulation, followed by a low-intensity regimen, may provide effective and safe secondary prophylaxis.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 68 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:763582 CAPLUS
DOCUMENT NUMBER: 128:10171
TITLE: The importance of initial heparin treatment on long-term clinical outcomes of antithrombotic therapy. The emerging theme of delayed recurrence
AUTHOR(S): Hull, Russell D.; Raskob, Gary E.; Brant, Rollin F.; Pineo, Graham F.; Valentine, Karen A.
CORPORATE SOURCE: Department of Medicine, the University of Calgary, Calgary, AB, Can.
SOURCE: Archives of Internal Medicine (1997), 157(20), 2317-2321
CODEN: AIMDAP; ISSN: 0003-9926
PUBLISHER: American Medical Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The relationship between initial heparin treatment and long-term clin.

outcome (late recurrence of thromboembolism) was evaluated in 3 consecutive, randomized, double-blind trials. The trials compared the use of continuous i.v. plus s.c. heparin, continuous i.v. heparin for 10 or 5 days, and continuous i.v. heparin with once-daily s.c. low -mol.-weight heparin. All the patients were followed up for 3 mo to assess the a priori hypothesis that inadequate initial heparin therapy could lead to recurrent venous thromboembolism during long-term therapy with warfarin sodium. The following were the rates of recurrent venous thromboembolism: continuous i.v. heparin, 3 (5.2%) of 58 patients vs. s.c. heparin, 11 (19.3%) of 57 patients; continuous i.v. heparin for 10 days, 7 (7.0%) of 100 patients or for 5 days, 7 (7.1%) of 99 patients; and continuous i.v. heparin, 15 (6.9%) of 219 patients vs. low-mol.-weight heparin, 6 (2.8%) of 213 patients. Pooled anal. of the results from patients treated with continuous i.v. heparin showed that of the total 32 patients with recurrent venous thromboembolism, in 6 patients thromboembolism occurred early (<10 days) and in 26 patients thromboembolism occurred late. Of these patients, the majority (20/32 [62.5%]) had therapeutic prothrombin time or international normalized ratio values before or at the time of the recurrent thromboembolic event. These findings demonstrate that the initial heparin treatment affects the long-term outcome. This conclusion applies when these data are analyzed for each individual study by treatment group, observed difference in outcome, and pooled anal.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 13 OF 68 MEDLINE on STN
ACCESSION NUMBER: 2003366372 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12899806
TITLE: Low-dose warfarin prevents recurrent thromboembolism.
AUTHOR: Plum Mary-Beth Fennell
CORPORATE SOURCE: Department of Pharmacy, School of Pharmacy, Virginia Commonwealth University, Richmond, USA.. mplum@vcu.edu
SOURCE: The Journal of family practice, (2003 Aug) Vol. 52, No. 8, pp. 588, 591.
Journal code: 7502590. ISSN: 0094-3509.
PUB. COUNTRY: United States
DOCUMENT TYPE: Commentary
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; PUBMED-NOT-MEDLINE
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 6 Aug 2003
Last Updated on STN: 30 Aug 2003
Entered Medline: 29 Aug 2003

AB Low-intensity warfarin (target international normalized ratio [INR], 1.5-2.0) effectively prevents recurrent venous thromboembolism without increasing the risk of major bleeding when used long-term for secondary prophylaxis. This is a reasonable approach following at least 3 to 12 months of full-intensity warfarin after the initial thromboembolic event.

L9 ANSWER 14 OF 68 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:417028 CAPLUS
DOCUMENT NUMBER: 141:64218
TITLE: Management of thrombophilia
AUTHOR(S): Bauer, K. A.
CORPORATE SOURCE: VA Boston Healthcare System and Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA,

USA
SOURCE: Journal of Thrombosis and Haemostasis (2003), 1(7), 1429-1434
CODEN: JTHOA5; ISSN: 1538-7933
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. It is now possible to identity acquired and hereditary risk factors in a substantial percentage of patients presenting with a venous thrombotic event. Discovery of the factor V Leiden and prothrombin G20210A mutations has greatly increased the percentage of patients in whom venous thrombosis can be attributed to hereditary thrombophilia. There is, however, considerable uncertainty as to how this information should be used in patient management. Although prolonged anticoagulation at an international normalized ratio of 2-3 is highly effective in preventing thrombotic recurrences, this benefit is partially offset by major bleeding which occurs at an average rate of 2%-3% per yr. A decision as to the overall benefit of extended anticoagulation in the individual patient requires assessment of the risk of recurrence in the absence of treatment vs. the bleeding risk associated with prolonged anticoagulation. Low-intensity warfarin therapy or novel anticoagulants such as oral direct thrombin inhibitors may prove effective strategies for preventing recurrent venous thromboembolism in patients with thrombophilia.
REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 15 OF 68 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:696572 CAPLUS
DOCUMENT NUMBER: 141:253480
TITLE: Appropriate level and length of postthrombotic warfarin treatment: An evaluation of recent developments
AUTHOR(S): ten Cate-Hoek, Arina J.; Prins, Martin H.
CORPORATE SOURCE: Department of Internal Medicine, Division of Hematology, University Hospital of Maastricht, Maastricht, Neth.
SOURCE: Current Opinion in Hematology (2004), 11(3), 182-186
CODEN: COHEF4; ISSN: 1065-6251
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Current treatment and secondary prophylaxis of venous thromboembolism has two major drawbacks. During vitamin K antagonist therapy, patients need to be monitored closely to maintain efficacy and minimize the bleeding risk due to fluctuations of the prothrombin time (international normalized ratio, INR), and after cessation of therapy there is the problem of recurrent thrombosis, ie, the catch-up phenomenon. Recent studies indicate that for most patients, vitamin K antagonist therapy aimed at an INR of 2.0 to 3.0 is optimal. For patients with thrombosis due to a temporary risk factor, extending treatment beyond 3 mo is not needed, whereas for other patients a minimal duration of 1 yr can be advocated. For patients with cancer, it is beneficial to postpone therapy with vitamin K antagonists and prolong initial low-mol.-weight therapy for 3 to 6 mo. New developments are aimed at further individualization of the duration of treatment and at the introduction of agents that are suitable for long-term treatment and do not require monitoring.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 16 OF 68 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:274860 CAPLUS
DOCUMENT NUMBER: 143:158
TITLE: The role of ximelagatran in the treatment of venous thromboembolism
AUTHOR(S): Schulman, Sam
CORPORATE SOURCE: Department of Haematology, Karolinska University Hospital, Stockholm, Swed.
SOURCE: Pathophysiology of Haemostasis and Thrombosis (2005), 34(Suppl. 1), 18-24
CODEN: PHTAC7; ISSN: 1424-8832
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Clin.-based evidence demonstrates that long-term oral anticoagulant therapy with the vitamin K antagonists is highly effective for the secondary prevention of venous thromboembolism (VTE). However, owing to fear of bleeding complications and the inconvenience of coagulation monitoring, many patients do not receive the required duration of treatment. This can lead to a high incidence of recurrent VTE events and has prompted the evaluation of alternative treatment strategies and the development of new anticoagulants for VTE management. For patient groups in which it is particularly difficult to maintain the target intensity of anticoagulation, low -mol.-weight heparin (LMWH) has been found to significantly reduce the risk of recurrent VTE without increasing bleeding risk. The parenteral administration of LMWH, however, is a drawback for long-term use in the outpatient setting. Long-term warfarin use at a lower intensity (international normalized ratio [INR] 1.5-2.0) has also been assessed as a possible strategy to reduce bleeding complications and the need for monitoring, but results were disappointing when compared with conventional-intensity warfarin (INR 2.0-3.0). New therapies in development that may potentially offer a more favorable benefit-risk profile and greater consistency and predictability of response include the synthetic pentasaccharides, fondaparinux and idraparinux. These parenterally administered indirect factor Xa inhibitors have a predictable pharmacokinetic profile, allowing use without coagulation monitoring. Fondaparinux to date has only been evaluated in the initial treatment (5-7 days) of symptomatic deep vein thrombosis. In contrast, idraparinux, with its longer half-life (80 h) allowing once-weekly parenteral dosing, has the potential for long-term treatment and is currently being assessed in phase III trials for the secondary prevention of VTE. Currently, the most promising new therapeutic option is the first of the oral direct thrombin inhibitors, ximelagatran. The THRombin Inhibitor in VEnous thromboembolism (THRIVE) clin. trial program has demonstrated that this agent is as effective as standard therapy for the acute treatment (THRIVE Treatment) and secondary prevention (THRIVE III) of VTE events and is well tolerated when used for 6 mo or over extended periods up to 1.5 years. Furthermore, with oral administration, fixed dosing and no requirement for anticoagulation monitoring, ximelagatran has the potential to facilitate optimal use and duration of VTE treatment by overcoming the limitations of current agents.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 17 OF 68 MEDLINE on STN
ACCESSION NUMBER: 1999173630 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10075308
TITLE: Current clinical concepts in perioperative anticoagulation.
AUTHOR: Hewitt R L; Chun K L; Flint L M
CORPORATE SOURCE: Department of Surgery, Tulane University School of Medicine, New Orleans, Louisiana 70112, USA.
SOURCE: The American surgeon, (1999 Mar) Vol. 65, No. 3, pp. 270-3.

Ref: 15
Journal code: 0370522. ISSN: 0003-1348.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 26 Apr 1999
Last Updated on STN: 26 Apr 1999
Entered Medline: 13 Apr 1999

AB Management of patients with significant risks for thromboembolism in the perioperative period requires consideration of both risks of thromboembolism and risks of anticoagulant therapy. Patients who are receiving warfarin therapy because of recent venous thromboembolism, nonvalvular atrial fibrillation, and mechanical heart valves are at increased risk during the interval when the warfarin is discontinued and when the international normalized ratio is at a subtherapeutic level.
In patients with an acute venous thromboembolic event within the past month, the use of intravenous heparin appears to be justified both preoperatively and postoperatively. If the venous thromboembolic event was within the past 2 to 3 months, use of intravenous heparin appears justified in the postoperative period. More than 3 months after an acute episode of venous thrombophlebitis, the relatively low risk of recurrence does not appear to justify the risks of complications from intravenous heparin. Patients with increased risks of arterial embolism, specifically those with nonvalvular atrial fibrillation and mechanical heart valves, are generally not at sufficient risk of arterial embolism to justify use of intravenous heparin during the perioperative subtherapeutic international normalized ratio interval when warfarin is withheld. A potential increased risk of recurrent arterial embolism when the preceding event was within a month suggests that elective surgery should be deferred beyond a month whenever possible in such patients. The use of fixed-dose, subcutaneous low molecular weight heparin has been observed to have advantages over use of unfractionated intravenous heparin both in terms of safety and efficiency. Further refinements in management of patients with significant risks of thromboembolism may occur with increased experience with low molecular weight heparin.

L9 ANSWER 18 OF 68 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:641378 CAPLUS
DOCUMENT NUMBER: 137:179307
TITLE: Current management of acute symptomatic deep vein thrombosis
AUTHOR(S): Heit, John A.
CORPORATE SOURCE: Division of Cardiovascular Diseases, Section of Vascular Diseases, Mayo Clinic and Foundation, Rochester, MN, USA
SOURCE: American Journal of Cardiovascular Drugs (2001), 1(1), 45-50
CODEN: AJCDDJ; ISSN: 1175-3277
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Venous thromboembolism is a common and potentially fatal disease. If properly used, anticoagulation therapy is effective in preventing recurrence of venous thromboembolism and in improving survival. Symptomatic patients with an objective diagnosis of acute deep vein thrombosis (DVT) or pulmonary embolism (PE) should receive immediate systemic heparin anticoagulation at dosages sufficient to rapidly prolong the activated

partial thromboplastin time into the laboratory-specific therapeutic range; this range corresponds to a plasma heparin concentration of 0.2 to 0.4 IU/mL (as measured by protamine sulfate titration), or 0.3 to 0.7 anti-Xa IU/mL. An oral vitamin K antagonist (e.g. warfarin) should be started within 24 h after starting heparin; the starting dose should be the estimated patient-specific daily dose with no loading dose. Heparin and warfarin anticoagulation should be overlapped for at least 4 to 5 days and until the international normalized ratio (INR) is within the therapeutic range (2.0 to 3.0) on 2 measurements made at least 24 h apart. The duration of warfarin anticoagulation should be individualized based on the resp. risks of venous thromboembolism recurrence and anticoagulant-related bleeding. In general, warfarin should be continued for at least 3 mo, and longer for patients with recurrent or idiopathic venous thromboembolism , malignant neoplasm, neurol. disease with extremity paresis, obesity, or laboratory evidence of a lupus anticoagulant/anticardiolipin antibody, homozygous carrier or combined heterozygous carrier for the factor V R506Q (Leiden) and prothrombin G20210A mutations, and possibly deficiency of either antithrombin, protein C, or protein S. Low mol. weight heparin (LMWH) is effective and well tolerated as acute therapy for patients with DVT or stable PE, and does not require laboratory monitoring or dose adjustment. Outpatient LMWH therapy is also well tolerated and cost effective for most patients with DVT, and possibly for selected patients with PE.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 19 OF 68 EMBASE

ACCESSION NUMBER: 1999108314 EMBASE

TITLE: A comparison of three months of anticoagulation with extended anticoagulation for a first episode of idiopathic venous thromboembolism.

AUTHOR: Kearon C.; Gent M.; Hirsh J.; Weitz J.; Kovacs M.J.; Anderson D.R.; Turpie A.G.; Green D.; Ginsberg J.S.; Wells P.; MacKinnon B.; Julian J.A.

CORPORATE SOURCE: Dr. C. Kearon, Hamilton Health Sciences Corporation, Henderson Division, 711 Concession St., Hamilton, Ont. L8V 1C3, Canada

SOURCE: New England Journal of Medicine, (25 Mar 1999) Vol. 340, No. 12, pp. 901-907. .
Refs: 25
ISSN: 0028-4793 CODEN: NEJMAG

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 Apr 1999
Last Updated on STN: 19 Apr 1999

AB Background: Patients who have a first episode of venous thromboembolism in the absence of known risk factors for thrombosis (idiopathic thrombosis) are often treated with anticoagulant therapy for three months. Such patients may benefit from longer treatment, however, because they appear to have an increased risk of recurrence after anticoagulant therapy is stopped. Methods: In this double-blind study, we randomly assigned patients who had completed 3 months of anticoagulant therapy for a first episode of idiopathic venous thromboembolism to continue receiving

warfarin, with the dose adjusted to achieve an international normalized ratio of 2.0 to 3.0, or to receive placebo for a further 24 months. Our goal was to determine the effects of extended anticoagulant therapy on rates of recurrent symptomatic venous thromboembolism and bleeding. Results: A prespecified interim analysis of efficacy led to the early termination of the trial after 162 patients had been enrolled and followed for an average of 10 months. Of 83 patients assigned to continue to receive placebo, 17 had a recurrent episode of venous thromboembolism (27.4 percent per patient-year), as compared with 1 of 79 patients assigned to receive warfarin (1.3 percent per patient-year, P<0.001). Warfarin resulted in a 95 percent reduction in the risk of recurrent venous thromboembolism (95 percent confidence interval, 63 to 99 percent). Three patients assigned to the warfarin group had nonfatal major bleeding (two had gastrointestinal bleeding and one genitourinary bleeding), as compared with none of those assigned to the placebo group (3.8 percent vs. 0 percent per patient-year, P=0.09). Conclusions: Patients with a first episode of idiopathic venous thromboembolism should be treated with anticoagulant agents for longer than three months.

L9 ANSWER 20 OF 68 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:879526 CAPLUS
DOCUMENT NUMBER: 137:362337
TITLE: Antithrombotic therapy and cancer
AUTHOR(S): Petralia, Gloria; Kakkar, Ajay K.
CORPORATE SOURCE: Imperial College, Hammersmith Hospital, London, UK
SOURCE: Fundamental and Clinical Cardiology (2003), 46(New Therapeutic Agents in Thrombosis and Thrombolysis (2nd Edition)), 103-115
CODEN: FCCAEH; ISSN: 1067-5264
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Thromboprophylaxis for patients undergoing surgery for cancer should include the use of graduated compression stockings associated with either unfractionated heparin (UFH) or low-mol.-weight heparin (LMWH). In patients receiving chemotherapy or radiotherapy, and considered to be at high risk for venous thromboembolism (VTE), thromboprophylaxis can be achieved by warfarin titrated to maintain an international normalized ratio (INR) between 1.3 and 1.9. The value of prophylaxis with LMWH in nonsurgical cancer patients is the subject of current prospective clin. trials. In cancer patients with central venous catheters, either the LMWH dalteparin 2500 once daily or the oral anticoagulant warfarin in a dose of 1 mg can be used for the prevention of line-associated thrombosis. Primary treatment of established VTE in those with cancer is identical with that recommended for noncancer patients (i.e., treatment with i.v. UFH or s.c. LMWH). Prevention of recurrent VTE is more difficult in the presence of malignant disease. Warfarin is the established first-line approach, failing which, UFH and LMWH are employed to prevent symptomatic recurrences.
REFERENCE COUNT: 87 THERE ARE 87 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 21 OF 68 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:356697 BIOSIS
DOCUMENT NUMBER: PREV200300356697
TITLE: Low-Intensity (INR 1.5-1.9) Versus Conventional-Intensity (INR 2.0-3.0) Anticoagulation for Extended Treatment of Unprovoked VTE: A Randomized Double

Blind Trial.

AUTHOR(S): Kearon, Clive [Reprint Author]; Ginsberg, Jeffrey S. [Reprint Author]; Kovacs, Michael [Reprint Author]; Anderson, David R. [Reprint Author]; Wells, Philip [Reprint Author]; Julian, Jim [Reprint Author]; MacKinnon, Betsy [Reprint Author]; Weitz, Jeffrey I. [Reprint Author]; Crowther, Mark A. [Reprint Author]; Dolan, Sean [Reprint Author]; Turpie, Alexander G. G. [Reprint Author]; Geerts, William H. [Reprint Author]; Solymoss, Susan [Reprint Author]; van Nguyen, Paul [Reprint Author]; Demers, Christine [Reprint Author]; Kahn, Susan [Reprint Author]; Kassis, Jeannine [Reprint Author]; Rodger, Marc [Reprint Author]; Hambleton, Julie [Reprint Author]; Gent, Michael [Reprint Author]

SOURCE: Blood, (November 16 2002). Vol. 100, No. 11, pp. Abstract No. 562. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 6 Aug 2003
Last Updated on STN: 6 Aug 2003

AB Background: Warfarin is very effective at preventing recurrent VTE but is associated with a substantial risk of bleeding. Indirect evidence suggests that, following 3 months of conventional therapy, a lower intensity of anticoagulation will be effective at preventing recurrent VTE and will cause less bleeding. Methods: We performed a multicentre, randomized, double blind, trial that compared low-intensity warfarin (international normalized ratio (INR) 1.5-1.9) with conventional-intensity warfarin (INR 2.0-3.0) for extended treatment of patients with unprovoked VTE. All patients had completed at least 3 months of initial conventional-intensity therapy. Results: 739 patients were randomized; 370 to low-intensity and 369 to conventional-intensity therapy. Average follow-up was 2.3 years. 16 low-intensity patients (1.9% per patient-year) and 5 conventional-intensity patients (0.6% per patient-year) had a recurrent VTE (hazard ratio: 3.3; 95% CI, 1.2 to 9.1). 8 low-intensity (0.96% per patient-year) and 8 conventional-intensity patients (0.93% per patient-year) had major bleeding (hazard ratio 1.0; 95% CI, 0.4 to 2.7). Major or minor bleeding occurred in 38 low-intensity patients (4.9% per patient-year) and 30 conventional-intensity patients (3.6% per patient-year) (hazard ratio 1.3; 95% CI, 0.8 to 2.1). Conclusion: Low-intensity warfarin was less effective than conventional-intensity warfarin for extended treatment of unprovoked VTE and was not associated with less bleeding.

L9 ANSWER 22 OF 68 EMBASE

ACCESSION NUMBER: 2003375175 EMBASE

TITLE: A comparison of two intensities of warfarin for the prevention of recurrent thrombosis in patients with the antiphospholipid antibody syndrome.

AUTHOR: Crowther M.A.; Ginsberg J.S.; Julian J.; Denburg J.; Hirsh J.; Douketis J.; Laskin C.; Fortin P.; Anderson D.; Kearon C.; Clarke A.; Geerts W.; Forgie M.; Green D.; Costantini L.; Yacura W.; Wilson S.; Gent M.; Kovacs M.J.

CORPORATE SOURCE: Dr. M.A. Crowther, St. Joseph's Hospital, 50 Charlton Ave.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

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DICTIONARY FILE UPDATES: 27 JUL 2006 HIGHEST RN 896463-29-9

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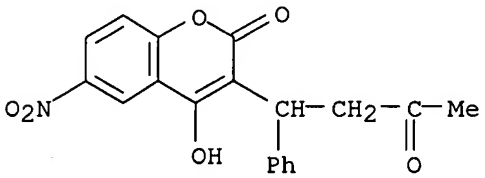
=> s warfarin
L1 74 WARFARIN

=> d 70-74

L1 ANSWER 70 OF 74 REGISTRY COPYRIGHT 2006 ACS on STN
RN 1641-04-9 REGISTRY
ED Entered STN: 16 Nov 1984
CN 2H-1-Benzopyran-2-one, 4-hydroxy-6-nitro-3-(3-oxo-1-phenylbutyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Coumarin, 3-(α-acetonylbenzyl)-4-hydroxy-6-nitro- (7CI, 8CI)
OTHER NAMES:
CN 3-(1α-Phenyl-β-acetylethyl)-4-hydroxy-6-nitrocoumarin
CN 6-Nitrowarfarin
FS 3D CONCORD
MF C19 H15 N O6
LC STN Files: CA, CAOLD, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L1 ANSWER 71 OF 74 REGISTRY COPYRIGHT 2006 ACS on STN
RN 152-72-7 REGISTRY
ED Entered STN: 16 Nov 1984
CN 2H-1-Benzopyran-2-one, 4-hydroxy-3-[1-(4-nitrophenyl)-3-oxobutyl]- (9CI)

(CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Acenocoumarol (6CI)
CN Coumarin, 3-(α-acetonyl-p-nitrobenzyl)-4-hydroxy- (8CI)
OTHER NAMES:
CN (±)-Acenocoumarin
CN (±)-Acenocoumarol
CN (±)-Nicoumalone
CN (±)-p-Nitrowarfarin
CN 3-(α-Acetonyl-4-nitrobenzyl)-4-hydroxycoumarin
CN 3-(α-Acetonyl-p-nitrobenzyl)-4-hydroxycoumarin
CN 3-(α-p-Nitrophenyl-β-acetylethyl)-4-hydroxycoumarin
CN 3-(Alpha-acetonyl-4-nitrobenzyl)-4-hydroxycoumarin
CN 3-[α-(4'-Nitrophenyl)-β-acetylethyl]-4-hydroxycoumarin
CN 3-[α-(p-Nitrophenol)-β-acetylethyl]-4-hydroxycoumarin
CN 3-[2-Acetyl-1-(p-nitrophenyl)ethyl]-4-hydroxycoumarin
CN 4-Hydroxy-2-oxo-3-[3-oxo-1-(4-nitrophenyl)butyl]-2H-chromene
CN Acenocoumarin
CN Ascumar
CN DL-3-(α-Acetonyl-4-nitrobenzyl)-4-hydroxycoumarin
CN G 23,350
CN G 23350
CN Minisintrom
CN Nicoumalone
CN Nitrowarfarin
CN Sincoumar
CN Sinkumar
CN Sinthrom
CN Sinthrome
CN Sintrom
CN Sintrom Mitis
CN Sintroma
CN Syncoumar
CN Syncumar
CN Syntrom
CN Trombostop
CN Zotil
FS 3D CONCORD
DR 70897-81-3
MF C19 H15 N O6
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, DDFU, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, PIRA, PROMT, PS, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
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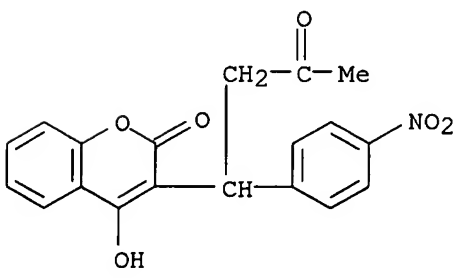
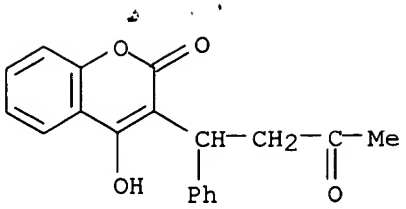


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

481 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
481 REFERENCES IN FILE CAPLUS (1907 TO DATE)
44 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L1 ANSWER 72 OF 74 REGISTRY COPYRIGHT 2006 ACS on STN
RN 129-06-6 REGISTRY
ED Entered STN: 16 Nov 1984
CN 2H-1-Benzopyran-2-one, 4-hydroxy-3-(3-oxo-1-phenylbutyl)-, sodium salt (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Coumarin, 3-(α-acetonylbenzyl)-4-hydroxy-, sodium salt (8CI)
CN Warfarin, sodium deriv. (6CI)
OTHER NAMES:
CN (±)-Warfarin sodium
CN 3-(α-Acetonylbenzyl)-4-hydroxycoumarin sodium
CN Aldocumar
CN Athrombin
CN Coumadan Sodico
CN Coumadin
CN Coumadin sodium
CN Coumadine
CN Coumafene sodium
CN Dimantil
CN Farin
CN Marevam
CN Marevan
CN Orfarin
CN Panwarfin
CN Prothromadin
CN Ratsul Soluble
CN Simarc 2
CN Sodium coumadin
CN Sodium warfarin
CN Sodium, [[2-oxo-3-(3-oxo-1-phenylbutyl)-2H-1-benzopyran-4-yl]oxy]-
CN Sofarin
CN Taro-warfarin
CN Tintorane
CN UniWarfin
CN Varfine
CN Waran
CN Warfarin sodium
CN Warfarin sodium salt
CN Warfarina
CN Warfil 5
CN Warfilone
CN Zoocoumarin sodium salt
DR 859043-62-2, 12795-55-0, 51821-81-9
MF C19 H16 O4 . Na
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, EMBASE, HSDB*, IMSCOSEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, PIRA, PROMT, PS, RTECS*, SCISEARCH, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
CRN (81-81-2)

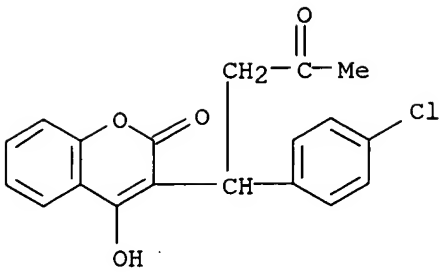


● Na

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

494 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
495 REFERENCES IN FILE CAPLUS (1907 TO DATE)
33 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L1 ANSWER 73 OF 74 REGISTRY COPYRIGHT 2006 ACS on STN
RN 81-82-3 REGISTRY
ED Entered STN: 16 Nov 1984
CN 2H-1-Benzopyran-2-one, 3-[1-(4-chlorophenyl)-3-oxobutyl]-4-hydroxy- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Coumachlor (6CI)
CN Coumarin, 3-(α-acetonyl-p-chlorobenzyl)-4-hydroxy- (7CI, 8CI)
OTHER NAMES:
CN (±)-3-(α-Acetonyl-4-chlorobenzyl)-4-hydroxy coumarin
CN (±)-Coumachlor
CN (±)-p-Chlorowarfarin
CN 3-(α-Acetonyl-4-chlorobenzyl)-4-hydroxycoumarin
CN 3-(α-p-Chlorophenyl-β-acetylethyl)-4-hydroxycoumarin
CN 3-[1-(p-Chlorophenyl)-2-acetylethyl]-4-hydroxycoumarin
CN Cumachlor
CN DL-3-(α-Acetonyl-4-chlorobenzyl)-4-hydroxycoumarin
CN Experimental Rodenticide 332
CN Geigy Rodenticide Exp. 332
CN p-Chlorowarfarin
CN Racemic coumachlor
CN Tomorin
FS 3D CONCORD
DR 128660-48-0, 95041-39-7
MF C19 H15 Cl O4
CI COM
LC STN Files: AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CSCHEM, DDFU, DRUGU, EMBASE, HSDB*, IPA, MEDLINE, MRCK*, MSDS-OHS, RTECS*, SPECINFO, TOXCENTER, ULIDAT, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

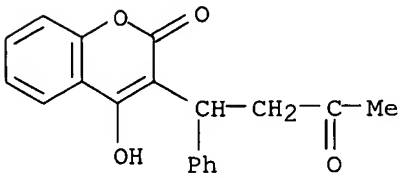


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

189 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
190 REFERENCES IN FILE CAPLUS (1907 TO DATE)
25 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L1 ANSWER 74 OF 74 REGISTRY COPYRIGHT 2006 ACS on STN
RN 81-81-2 REGISTRY
ED Entered STN: 16 Nov 1984
CN 2H-1-Benzopyran-2-one, 4-hydroxy-3-(3-oxo-1-phenylbutyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Coumarin, 3-(α-acetonylbenzyl)-4-hydroxy- (7CI, 8CI)
OTHER NAMES:
CN (±)-Warfarin
CN (±)-Warfarin-alcohol
CN (RS)-Warfarin
CN 1-(4'-Hydroxy-3'-coumarinyl)-1-phenyl-3-butanone
CN 3-(α-Acetonylbenzyl)-4-hydroxycoumarin
CN 3-(α-Phenyl-β-acetylethyl)-4-hydroxycoumarin
CN 3-(1'-Phenyl-2'-acetylethyl)-4-hydroxycoumarin
CN 4-Hydroxy-3-(3-oxo-1-phenylbutyl)-2H-chromen-2-one
CN Athrombine-K
CN Brumolin
CN Co-Rax
CN Compound 42
CN Coumafen
CN Coumafene
CN Coumaphen
CN Coumefene
CN Dethmor
CN DL-3-(α-Acetonylbenzyl)-4-hydroxycoumarin
CN Kumader
CN Kumadu
CN Kumatox
CN NSC 59813
CN rac-Warfarin
CN Ratron
CN Ratron G
CN Rodafarin
CN Rodafarin C
CN Rodex
CN Temus W
CN Vampirinip II
CN Vampirinip III
CN W.A.R.F. 42
CN Warf 5
CN WARF compound 42
CN Warfarin

CN Zoocoumarin
FS 3D CONCORD
DR 56573-89-8, 5543-56-6
MF C19 H16 O4
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, PIRA, PROMT, PS, RTECS*, SCISEARCH, SPECINFO, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4057 REFERENCES IN FILE CA (1907 TO DATE)
57 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
4064 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

E., Hamilton, Ont. L8N 4A6, Canada. crowthrm@mcmaster.ca
SOURCE: New England Journal of Medicine, (18 Sep 2003) Vol. 349, No. 12, pp. 1133-1138. .
Refs: 10
ISSN: 0028-4793 CODEN: NEJMAG
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
018 Cardiovascular Diseases and Cardiovascular Surgery
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 2 Oct 2003
Last Updated on STN: 2 Oct 2003

AB Many patients with the antiphospholipid antibody syndrome and recurrent thrombosis receive doses of warfarin adjusted to achieve an international normalized ratio (INR) of more than 3.0. However, there are no prospective data to support this approach to thromboprophylaxis. METHODS We performed a randomized, double-blind trial in which patients with antiphospholipid antibodies and previous thrombosis were assigned to receive enough warfarin to achieve an INR of 2.0 to 3.0 (moderate intensity) or 3.1 to 4.0 (high intensity). Our objective was to show that high-intensity warfarin was more effective in preventing thrombosis than moderate-intensity warfarin. RESULTS A total of 114 patients were enrolled in the study and followed for a mean of 2.7 years. Recurrent thrombosis occurred in 6 of 56 patients (10.7 percent) assigned to receive high-intensity warfarin and in 2 of 58 patients (3.4 percent) assigned to receive moderate-intensity warfarin (hazard ratio for the high-intensity group, 3.1; 95 percent confidence interval, 0.6 to 15.0). Major bleeding occurred in three patients assigned to receive high-intensity warfarin and four patients assigned to receive moderate-intensity warfarin (hazard ratio, 1.0; 95 percent confidence interval, 0.2 to 4.8). High-intensity warfarin was not superior to moderate-intensity warfarin for thromboprophylaxis in patients with antiphospholipid antibodies and previous thrombosis. The low rate of recurrent thrombosis among patients in whom the target INK was 2.0 to 3.0 suggests that moderate-intensity warfarin is appropriate for patients with the antiphospholipid antibody syndrome.

L9 ANSWER 23 OF 68 EMBASE
ACCESSION NUMBER: 1998153808 EMBASE
TITLE: Anticardiolipin antibodies predict early recurrence of thromboembolism and death among patients with venous thromboembolism following anticoagulant therapy.
AUTHOR: Schulman S.; Svenungsson E.; Granqvist S.
CORPORATE SOURCE: Dr. S. Schulman, Coagulation Unit, Department of Medicine, Karolinska Hospital, S-171 76 Stockholm, Sweden
SOURCE: American Journal of Medicine, (1998) Vol. 104, No. 4, pp. 332-338. .
Refs: 22
ISSN: 0002-9343 CODEN: AJMEAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
026 Immunology, Serology and Transplantation
037 Drug Literature Index

LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 18 Jun 1998
Last Updated on STN: 18 Jun 1998

AB PURPOSE: To compare the risk of recurrent venous thromboembolism in patients with and without antiphospholipid antibodies. PATIENTS AND METHODS: Anticardiolipin antibodies were tested 6 months after a first or second episode of venous thromboembolism. Of the patients with a first episode of venous thromboembolism only the 412 who received 6 months of anticoagulation were studied. Two hundred and eleven patients with a second episode received oral anticoagulation for 6 months or indefinitely. The therapy was targeted at an international normalized ratio (INR) of 2.0 to 2.85. All patients were followed up for 4 years after enrollment. RESULTS: Among the 412 patients with a first episode of venous thromboembolism the risk of recurrence was 29% in patients with anticardiolipin antibodies and 14% in those without antibodies (P = 0.0013). In those with antibodies, there was an increased risk during the first 6 months after cessation of anticoagulation. The risk of recurrence increased with the titer of the antibodies. Four-year mortality rate was 15% in those with antibodies and 6% in those without (P = 0.01). Among 34 patients with a second event of venous thromboembolism and anticardiolipin antibodies, there were no recurrences during anticoagulant therapy versus 20% in those who received only 6 months of treatment (P = 0.08). CONCLUSIONS: The presence of elevated titers of anticardiolipin antibodies 6 months after an episode of venous thromboembolism is a predictor for an increased risk of recurrence and of death. Patients with anticardiolipin antibodies and venous thromboembolism seem to benefit from prolonged oral anticoagulation.

L9 ANSWER 24 OF 68 MEDLINE on STN
ACCESSION NUMBER: 2005278138 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15869591
TITLE: Poor anticoagulation quality in the first 3 months after unprovoked venous thromboembolism is a risk factor for long-term recurrence.
AUTHOR: Palareti G; Legnani C; Cosmi B; Guazzaloca G; Cini M; Mattarozzi S
CORPORATE SOURCE: Department of Angiology & Blood Coagulation Marino Golinelli, University Hospital S. Orsola-Malpighi, Bologna, Italy.. palareti@tin.it
SOURCE: Journal of thrombosis and haemostasis : JTH, (2005 May) Vol. 3, No. 5, pp. 955-61.
Journal code: 101170508. ISSN: 1538-7933.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200508
ENTRY DATE: Entered STN: 1 Jun 2005
Last Updated on STN: 20 Aug 2005
Entered Medline: 19 Aug 2005

AB BACKGROUND AND AIM: Several factors are associated with an increased risk of recurrent venous thromboembolism (VTE). The aim of the study was to investigate whether the quality of oral anticoagulation therapy (OAT) is a long-term risk factor for recurrence of VTE after OAT interruption. METHODS AND RESULTS: A total of 297 patients (170 males) with a recent acute unprovoked VTE episode were prospectively monitored during OAT in our anticoagulation clinic and followed up for 21 months after OAT interruption. Recurrent events were recorded in 42 subjects for 493 years of follow-up [14.1% of patients; 8.5%

patient-years (pt-y)] after OAT withdrawal. The rate of recurrence was not correlated to OAT duration. Subjects experiencing recurrence after OAT interruption had spent significantly more time at markedly subtherapeutic international normalized ratio (INR) levels (<1.5) and less time within the therapeutic range (2.0-3.0 INR) during OAT. Relative risk (RR) of recurrence was significantly higher [2.77 (95% confidence interval (CI) 1.49-5.18; P = 0.001) and 2.70 (95% CI 1.39-5.25; P = 0.003) at univariate and multivariate analysis, respectively] in those who spent more time (upper quintile) at INR values <1.5, being especially evident in the first 90 days of OAT. RR was significantly higher at univariate [2.05 (95% CI 1.07-3.96; P = 0.031)] but not at multivariate [1.98 (95% CI 0.98-4.0; P = 0.056)] analysis when the entire OAT period was considered. Subjects in the upper quintile of time spent at INR values <1.5 had significantly higher D-dimer values when OAT was stopped and after 3 months. CONCLUSIONS: The amount of time that subjects with an acute unprovoked VTE event spend at near-normal INR values (<1.5) during the first 3 months of treatment is associated with higher D-dimer values measured during OAT and after its interruption and is a significant risk factor for late VTE recurrence.

L9 ANSWER 25 OF 68 EMBASE

ACCESSION NUMBER: 94246534 EMBASE
DOCUMENT NUMBER: 1994246534
TITLE: Quality of oral anticoagulant control and treatment in Sweden.
AUTHOR: Schulman S.; Carlsson A.; Gustafsson C.; Grondahl A.; Rhedin A.-S.; Tornebohm E.; Johansson M.; Lockner D.; Lindmarker P.; Johnsson H.; Nicol P.; Kobosko J.; Malmros B.; Arcini N.; Saaw J.; Loogna E.; Stig R.; Viering S.; Ljungberg B.; et al.
CORPORATE SOURCE: National Haemophilia Centre, Sheba Medical Centre,52621 Tel-Hashomer, Israel
SOURCE: Journal of Internal Medicine, (1994) Vol. 236, No. 2, pp. 143-152. .
ISSN: 0954-6820 CODEN: JINMEO
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 31 Aug 1994
Last Updated on STN: 31 Aug 1994

AB Objectives. To define laboratory-dependent and clinical factors that negatively influence the precision and safety of oral anticoagulation and to determine whether this creates differences in clinical outcome between the participating hospitals. Design. Laboratory. The clinical chemistry laboratories of participating hospitals performed prothrombin time tests on blinded, standardized plasma samples on six occasions. Clinical. Patients with a first or second episode of venous thromboembolism were randomized to different durations of oral anticoagulation; the target was an international normalized ratio (INR) of 2.0-2.85. Setting. Multicentre study at the departments of medicine of 16 Swedish hospitals. Subjects. In total, 1124 patients with venous thromboembolism were followed for 600 patient-years of oral anticoagulation. Main exclusion criteria were previously known malignancy or venous ulcer, known congenital deficiency of an inhibitor of coagulation and unwillingness to participate. Main outcome measures.

Laboratory. Interlaboratory variation was measured with coefficient of variation. Clinical. End-points were recurrent venous thromboembolism and haemorrhages requiring hospitalization or treatment with blood products or vitamin K. Results. Laboratory. The interlaboratory variation in prothrombin time analyses was 11.3% at a mean INR of 3.8. No difference was detected between laboratories using the two prevalent thromboplastin reagents in Sweden or between those using the Behnk Coagulator and ACL instruments. INR results. Seventy-five per cent of the INR values were ≥2.0, and 58% were within the target range. The time spent within the target range was between 57 and 74% at the worst and best hospital, respectively. Referral of patients to satellite clinics and fear of treating patients living in distant villages too intensively were factors that decreased the number of effectively anticoagulated patients. The percentage of patients effectively anticoagulated was lower amongst those <50 than those ≥50 years of age and also lower during the 1st year than during the 2nd and 3rd. Clinical events. There were eight objectively verified events of recurrent venous thromboembolism [1.3 in 100 patient-years or 0.7%; 95% confidence limits (CL): 0.2, 1.2]. Seventeen haemorrhagic events occurred, corresponding to 2.8 per 100 patient-years or 1.5% (CL: 0.8, 2.2); two fatal haemorrhages corresponding to 0.3 per 100 patient-years or 0.2% (CL: 0.0, 0.4). The difference in the incidence of these complications between hospitals with >60 and ≤60% of patients effectively anticoagulated did not reach statistical significance. Patients with haemorrhagic complications were not older than the rest. Conclusions. The performance of the laboratories was acceptable. Clinically important differences between the hospitals were not observed. The incidences of thromboembolic and haemorrhagic complications were low, even in comparison with other randomized trials concerning venous thromboembolism. However, it might be possible to reduce the risk of haemorrhage further with increased centralization and improved education of patients as well as medical staff, and perhaps to reduce the risk of recurrent venous thromboembolism by aiming at a more intensive range of anticoagulation during the 1st month.

L9 ANSWER 26 OF 68 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:909522 CAPLUS
DOCUMENT NUMBER: 142:189920
TITLE: The pharmacology and management of the vitamin K antagonists: the seventh ACCP conference on antithrombotic and thrombolytic therapy
AUTHOR(S): Ansell, Jack; Hirsh, Jack; Poller, Leon; Bussey, Henry; Jacobson, Alan; Hylek, Elaine
CORPORATE SOURCE: USA
SOURCE: Chest (2004), 126(3, Suppl.), 204S-233S
CODEN: CHETBF; ISSN: 0012-3692
PUBLISHER: American College of Chest Physicians
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. This article concerning the pharmacokinetics and pharmacodynamics of vitamin K antagonists (VKAs) is part of the Seventh American College of Chest Physicians Conference on Antithrombotic and Thrombolytic Therapy: Evidence-Based Guidelines. The article describes the antithrombotic effect of VKAs, the monitoring of anticoagulation intensity, the clin. applications of VKA therapy, and the optimal therapeutic range of VKAs, and provides specific management recommendations. Grade 1 recommendations are strong, and indicate that the benefits do, or do not, outweigh the risks, burdens, and costs. Grade 2 suggests that individual patient's values may load to different choices (for a full understanding of the grading see Guyatt et al, CHEST 2004; 126:1795-1875). Among the key recommendations in this article are the following: for dosing of VKAs, we suggest the initiation of oral

anticoagulation therapy with doses between 5 and 10 mg for the first 1 or 2 days for most individuals, with subsequent dosing based on the international normalized ratio (INR) response (Grade 2B). In the elderly and in other patient subgroups with an elevated bleeding risk, we suggest a starting dose at ≤ 5 mg (Grade 2C). We recommend basing subsequent doses alter the initial two or three doses on the results of INR monitoring (Grade 1C). The article also includes several specific recommendations for the management of patients with INRs above the therapeutic range and for patients requiring invasive procedures. For example, in patients with mild to moderately elevated INRs without major bleeding, we suggest that when vitamin K is to be given it be administered orally rather than s.c. (Grade 1A). Fur the management of patients with a low risk of thromboembolism, we suggest slopping warfarin therapy approx. 4 days before they undergo surgery (Grade 2C). For patients with a high risk of thromboembolism, we suggest stopping warfarin therapy approx. 4 days before surgery, to allow the INR to return to normal, and beginning therapy with full-dose unfractionated heparin or full-dose low-mol.-weight heparin as the INR falls (Grade 2C). In patients undergoing dental procedures, we suggest the use of tranexamic acid mouthwash (Grade 2B) or epsilon amino caproic acid mouthwash without interrupting anticoagulant therapy (Grade 2B) if there is a concern for local bleeding. For most patients who have a lupus inhibitor, we suggest a therapeutic target INR of 2.5 (range, 2.0 to 3.0) [Grade 2B]. In patients with recurrent thromboembolic events with a therapeutic INR or other addnl. risk factors, we suggest a target INR of 3.0 (range, 2.5 to 3.5) [Grade 2C]. As models of anticoagulation monitoring and management, we recommend that clinicians incorporate patient education, systematic INR testing, tracking, and follow-up, and good communication with patients concerning results and dosing decisions (Grade 1C+).

REFERENCE COUNT: 327 THERE ARE 327 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 27 OF 68 MEDLINE on STN

ACCESSION NUMBER: 2005278317 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15922694

TITLE: Oral anticoagulation strategies after a first idiopathic venous thromboembolic event.

AUTHOR: Aujesky Drahomir; Smith Kenneth J; Roberts Mark S

CORPORATE SOURCE: Division of General Internal Medicine, Department of Medicine, University of Pittsburgh, Pennsylvania, USA.. aujesky@swissonline.ch

SOURCE: The American journal of medicine, (2005 Jun) Vol. 118, No. 6, pp. 625-35.
Journal code: 0267200. ISSN: 0002-9343.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200506

ENTRY DATE: Entered STN: 1 Jun 2005
Last Updated on STN: 24 Jun 2005
Entered Medline: 23 Jun 2005

AB PURPOSE: The optimal duration and intensity of warfarin therapy after a first idiopathic venous thromboembolic event are uncertain. We used decision analysis to evaluate clinical and economic outcomes of different anticoagulation strategies with warfarin. METHODS: We built a Markov model to assess 6 strategies to treat 40- to 80-year-old men and women after their first idiopathic venous thromboembolic event: 3-month, 6-month, 12-month, 24-month, and unlimited-duration conventional-intensity anticoagulation (International Normalized Ratio, 2-3) and unlimited-duration

low-intensity anticoagulation (International Normalized Ratio, 1.5-2). The model incorporated age- and sex-specific clinical parameters, utilities, and costs. Using a societal perspective, we compared strategies based on quality-adjusted life-years (QALYs), lifetime costs, and incremental cost-effectiveness ratios. RESULTS: In our baseline analysis, incremental cost-effectiveness ratios were lower in younger patients and in men, reflecting the higher bleeding risk at older ages, and the lower risk of recurrence among women. Based on a willingness-to-pay of <$50000/QALY, the 24-month strategy was most cost-effective in 40-year-old men ($48805/QALY), while the 6-month strategy was preferred in 40-year-old women ($35977/QALY) and 60-year-old men ($29878/QALY). In patients aged >/=80 years, 3-month anticoagulation was less costly and more effective than other strategies. Cost-effectiveness results were influenced by the risks associated with recurrent venous thromboembolism, the major bleeding risk of conventional-intensity anticoagulation and the disutility of taking warfarin. CONCLUSION: Longer initial conventional-intensity anticoagulation is cost-effective in younger patients while 3 months of anticoagulation is preferred in elderly patients. Patient age, sex, clinical factors, and patient preferences should be incorporated into medical decision making when selecting an appropriate anticoagulation strategy.

L9 ANSWER 28 OF 68 MEDLINE on STN
ACCESSION NUMBER: 2006033452 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16420110
TITLE: A pilot study of home treatment of deep vein thrombosis with subcutaneous once-daily enoxaparin plus warfarin.
AUTHOR: Bishop Beverly; Wilson Andrew G; Post Douglas; Howard Laureen; Ruehlen Lawrence
CORPORATE SOURCE: Saint Joseph's Health System, Clinton Township, MI 48038, USA.. bishobp@trinity-health.org
SOURCE: Journal of managed care pharmacy : JMCP, (2006 Jan-Feb) Vol. 12, No. 1, pp. 70-5.
Journal code: 9605854. ISSN: 1083-4087.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200605
ENTRY DATE: Entered STN: 20 Jan 2006
Last Updated on STN: 17 May 2006
Entered Medline: 16 May 2006

AB OBJECTIVE: To evaluate patient satisfaction, effectiveness, and safety of at-home treatment of acute deep vein thrombosis (DVT) with subcutaneous enoxaparin dosed at 1.5 mg/kg once daily plus oral warfarin. METHODS: Patients with acute DVT and no more than 1 previous episode of DVT received enoxaparin plus oral warfarin until their international normalized ratio (INR) was >2 on 2 consecutive days. Patients were recruited between November 2000 and June 2003, and a home-care nurse visited the patient daily to administer the enoxaparin and to perform a fingerstick INR test. Patients received warfarin at doses adjusted to maintain an INR in the range of 2 to 3. Efficacy and safety were assessed daily by a home-care nurse and then by telephone interview conducted by a pharmacist at 14, 30, and 90 days during follow-up. Patient satisfaction with treatment was assessed by a verbal questionnaire. RESULTS: There were 52 patients enrolled. The mean duration of enoxaparin home treatment was 4.5 days, and the mean INR on discontinuation of enoxaparin was 2.73. Most patients (84.6%) had INRs within the desired therapeutic range (INR value 2-3); no patient had a subtherapeutic INR. There were no symptoms of recurrent venous thromboembolism reported. Major bleeding

occurred 7 days after discontinuation of enoxaparin in one patient with impending surgery for removal of a uterine tumor. There were 2 cases of minor bleeding. The patient satisfaction questionnaire revealed that patients considered home treatment to be acceptable. The average cost savings was $2,925 per patient compared with typical inpatient treatment with unfractionated heparin. CONCLUSION: The results of this pilot study suggest that home treatment with initial once-daily enoxaparin in conjunction with long-term oral warfarin is a safe and effective alternative to inpatient therapy with once-daily enoxaparin or unfractionated heparin for select patients with acute DVT. Cost savings are derived from the substitution of inpatient care with home care.

L9 ANSWER 29 OF 68 MEDLINE on STN
ACCESSION NUMBER: 2004430569 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15336480
TITLE: Management patterns and outcomes of patients with venous thromboembolism in the usual community practice setting.
AUTHOR: Willey Vincent J; Bullano Michael F; Hauch Ole; Reynolds Matthew; Wygant Gail; Hoffman Lauren; Mayzell George; Spyropoulos Alex C
CORPORATE SOURCE: HealthCore, Inc., Wilmington, DE 19081, USA.. vwilley@healthcore.com
SOURCE: Clinical therapeutics, (2004 Jul) Vol. 26, No. 7, pp. 1149-59.
Journal code: 7706726. ISSN: 0149-2918.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200411
ENTRY DATE: Entered STN: 1 Sep 2004
Last Updated on STN: 9 Nov 2004
Entered Medline: 8 Nov 2004
AB OBJECTIVE: The objectives of this study were to observe a commercially insured sample diagnosed with a venous thromboembolism

Day : Friday
Date: 7/28/2006
Time: 12:43:18

PALM INTRANET

Inventor Information for 10/767758

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